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EXAMINER	
BECKHARDT, LYNDSEY MARIE	
ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
08/04/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,932	GAZZA, GIANLUCA	
	Examiner	Art Unit	
	LYNDSEY BECKHARDT	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *8,10,17,27 and 32-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,11-16,18-26 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/02/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-41 are currently pending. Claims 1-7, 9, 11-16, 18-26 and 28-31 are currently pending and under examination.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-32) in the reply filed on 06/22/2009 is acknowledged.

Claims 33-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/22/2009.

Applicant's election of Hydrophobic hydrocarbon for polymer, Vacuum for Pressure, Gas for polymer form, Hydrophobic hydrocarbon for drug containing polymer, 4-[4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-phenyl]benzamide methansulphonate for drug and hyaluronic acid for biological molecule in the reply filed on 06/22/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8, 10, 17, 27 and 32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/22/2009.

Priority

The instant application is a national stage entry of PCT/IB03/05003, filed 11/07/2003. The effective filing date for claims 1-41 is 11/07/2003.

Information Disclosure Statement

Applicant's Informational Disclosure Statement, filed on 05/02/2006 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (Water-soluble poly(acrylamide-allylamide) derivatives of saccharides for protein-saccharide binding studies, publication date: 1995) and US 2002/0037874 (publication date 03/27/2002).

The '877 publication teaches an example of a biopolymer is hyaluronic acid ("HA"), a naturally occurring mucopolysaccharide (page 1, paragraph [0002]). The biologically active conjugate of this invention is useful as a drug delivery vehicle for the in-vivo delivery of the therapeutic proteins to specific cells, organs or tissue in a subject (page 2, paragraph [0013]). A biopolymer, such as hyaluronic acid, can be immobilized onto the surface of a substrate which has been modified to contain, for instance, exposed amino groups, which can be reacted with Traut's reagent and then HA-NEA (page 6, paragraph [0052]). The aminated surface, prepared, for instance by cold plasma deposition of an allyl amine, is treated with a reagent, such as Traut's reagent, to convert the amino groups into free thiol groups. The derivatized surface is then reacted with Ha-NEA to immobilize HA to the surface by a disulfide bond (page 7, paragraph [0053]).

The ‘877 publication does not teach a polymer having active functional groups capable of chemically binding biological molecules, wherein the application takes place in a single step. The ‘877 publication does not teach application of the polymer to a medical device.

Klein teaches two types of coupling reaction were used to prepare polyacrylamide derivatives of saccharides: reductive amination was applied to couple the reducing dissacharides and a carboiimide reaction was used to couple heparin via its carboxyl groups to the amino groups (abstract).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to react a biological molecule containing carboxyl groups, such as heparin, as taught by Klein on the cold plasma allyl amine treated surface as taught by the '877 publication because the carboxyl group in heparin can react with an amino group as taught by Klein. One would have been motivated to directly react the biological molecule containing carboxyl groups without the use of Traut's reagent because it would require less steps to produce the biological molecule coating.

The ‘874 publication teaches a novel sulphated compound of hyaluronic acid and derivatives thereof. The compound of the invention have anticoagulant and antithrombotic activities and are useful in the preparation of pharmaceutical compositions and biomaterial and in the production of coatings for biomaterials compositions and in the production of coating for biomedical object (abstract). The

biomaterials can be used to advantage in various fields of surgery: such as vascular stents (page 3, paragraph [0034]).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the hyaluronic coating on a substrate as taught by the ‘877 publication for a biomedical application such as a stent because it has anticoagulant and antithrombotic activity as taught by the '874 publication.

Regarding claim 1, the limitation of a polymer having active functional groups capable of chemically binding biological molecules, characterized in that said application takes place in a single step by means of cold plasma methods is obvious over a biopolymer, such as hyaluronic acid, can be immobilized onto the surface of a substrate which has been modified to contain, for instance, exposed amino groups, which can be reacted with Traut's reagent and then HA-NEA (page 6, paragraph [0052]). The aminated surface, prepared, for instance by cold plasma deposition of an allyl amine, is treated with a reagent, such as Traut's reagent, to convert the amino groups into free thiol groups. The derivatized surface is then reacted with Ha-NEA to immobilize HA to the surface by a disulfide bond (page 7, paragraph [0053]) as taught by the ‘877 publication in combination with reductive amination was applied to couple the reducing dissacharides and a carboiimide reaction was used to couple heparin via its carboxyl groups to the amino groups (abstract) as taught by Klein. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to react a biological molecule containing carboxyl groups, such as heparin, as taught by Klein on the cold plasma allyl amine treated surface as taught by the '877

publication because the carboxyl group in heparin can react with an amino group as taught by Klein. One would have been motivated to directly react the biological molecule containing carboxyl groups without the use of Traut's reagent because it would require less steps to produce the biological molecule coating.

The limitation of preparing a drug eluting medical device is obvious over the teaching of the combination of the '877 publication and Klein as taught above in combination with the teachings of hyaluronic acid and derivatives having anticoagulant and anithrombotic activities and used on biomedical objects such as stents as taught by the '874 publication. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the hyaluronic coating on a substrate as taught by the '877 publication for a biomedical application such as a stent because it has anticoagulant and antithrombotic activity as taught by the '874 publication.

Regarding claims 2 and 3, the limitation of said polymers being chosen from among polymers having amine groups, carboxyl groups and sulphhydril groups and wherein the polymers having amine groups are chosen from among allylamine, heptylamine, aliphatic amines and aromatic amines is obvious over the aminated surface, prepared, for instance by cold plasma deposition of an allyl amine (page 7, paragraph [0053]) as taught by the '877 publication.

Regarding claims 25 and 26, the limitations of depositing biological molecules on the surface of said polymer having stable reactive functional groups and said biological molecules are chosen from among anit-thrombotic substances and hyaluronic acid (the elected species) is obvious over A biopolymer, such as hyaluronic acid, can be

immobilized onto the surface of a substrate which has been modified to contain, for instance, exposed amino groups (page 6, paragraph [0052]) as taught by the '877 publication.

Claims 6-7, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (Water-soluble poly(acrylamide-allylamide) derivatives of saccharides for protein-saccharide binding studies, publication date: 1995) and US 2002/0037874 (publication date 03/27/2002) as applied to claims 1-3 and 25-26 above, and further in view of US 4,720,512 (patent date: 01/19/1988).

As mentioned in the above 103(a) rejection, all the limitations of claims 1-3 and 25-26 are taught by the combination of the '877 publication, Klein and the '874 publication. The combination of references does not teach the cold plasma as under vacuum at a pressure of 0.01 and 10 mbar at 1 to 500 W and for not more than 30 minutes. The polymer is not taught in the form of a gas or being deposited at a thickness of 0.01 to 10 microns.

The '512 patent teaches a method for preparing antithrombogenic polymeric articles bonded to the polymeric surface to provide increased antithrombogenic activity (column 1, lines 6-13). It would be desirable to provide a material which has excellent biological and chemical stability towards body fluids, namely blood, and which retains its antithrombogenic agent and antibiotic effect for a long term while being slowly leachable when in contact with blood (column 2, lines 40-46). Bonding of moieties to the

polymeric substrate surface is accomplished via glow discharge (ionized gas) treatment. This process is generally referred to in the art as plasma treatment. Plasma treatment is accomplished using a glow discharge ionization chamber, whereby samples are placed in the chamber and the chamber pressure is reduced to a minimal level, e.g. 0.1 torr or less, via vacuum pump. The fluorine, siloxane, silane and/or silazane compounds are introduced in gaseous form in to the plasma chamber to a desired level, e.g. about 0.3 torr and purged to about 0.1 torr. Radio frequency power is then generated and applied to the gas in the chamber for a fixed period of time. For example, about 10 to 100 watts might be applied for a period of about 10 to about 20 minutes (column 4, lines 35-57). The antithrombogenic materials may be selected form the group consisting of heparin, prostaglandins, sulfated polysaccharides ad mixtures thereof (column 5, lines 37-43).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the cold plasma treatment conditions as taught by the '512 patent to deposit the allylamine to the substrate surface to which hyaluronic acid can bind as taught by the combination of the '877 publication, Klein and the '874 publication because the cold plasma deposition method is well known in the art and used to apply functional groups to a polymer to which sulfated polysaccharides can bind as taught by the '512 patent.

Regarding claim 6, the limitation of the cold plasma method being produced under vacuum using discontinuous or continuous technology is obvious over plasma treatment is accomplished using a glow discharge ionization chamber, whereby

samples are placed in the chamber and the chamber pressure is reduced to a minimal level, e.g. 0.1 torr or less, via vacuum pump. The fluorine, siloxane, silane and/or silazane compounds are introduced in gaseous form in to the plasma chamber to a desired level, e.g. about 0.3 torr and purged to about 0.1 torr. Radio frequency power is then generated and applied to the gas in the chamber for a fixed period of time (column 4, lines 40-55) as taught by the ‘512 patent.

Regarding claim 7, the limitation where the cold plasma vacuum pressure is between 0.01 and 10 mbar, at a power between 1 and 500 W and for a period of time of not more than 30 minutes is obvious over the vacuum minimal level is 0.1 torr, where pressure of about 0.1 to 5 torrs is desired, the power is applied for a fixed time, for example 10 to 100 watts for about 10 to 20 minutes (column 4, lines 43-56). The 0.1 to 5 torrs taught by the '512 publication is equivalent to 0.133 to 6.66 mbar, which falls within the range required by the instant claims.

Regarding claim 9, the limitation in which the precursor of said polymer is in the form of a gas is obvious over the compounds are introduced in gaseous form into the plasma chamber to a desired level as taught by the '512 publication. The compounds taught by the ‘512 publication are not the same as allylamine polymer precursor taught to be deposited by cold plasma by the combination of the ‘877 publication, Klein and the ‘874 publication, however it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to introduce the allylamine polymer in the form of a gas for cold plasma deposition.

Regarding claim 11, the limitation where said polymer is applied in the form of a film with a thickness of between 0.01 and 10 microns would be met by the conditions used in the cold plasma deposition as taught by the '512 patent being the same as those disclosed in the instant application. One of ordinary skill in the art at the time the invention was made would have expected the same polymer precursor deposited at the same pressure, power and time would have the same coating thickness. The coating thickness would also be optimized by one of ordinary skill in the art at the time the invention was made to obtain the intended results of the coating. The recited variants would have been obvious unless there is evidence of the criticality or unexpected results.

Claims 4, 11-13, 15-16, 18-19, 28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (Water-soluble poly(acrylamide-allylamide) derivatives of saccharides for protein-saccharide binding studies, publication date: 1995) and US 2002/0037874 (publication date 03/27/2002) as applied to claims 1-3 and 25-26 above, and further in view of US 6,335,029 (patent date: 01/01/2002).

As mentioned in the above 103(a) rejection, all the limitations of claims 1-3 and 25-26 are taught by the combination of the '877 publication, Klein and the '874 publication. The combination of references does not teach the precursor polymer being chosen from acrylic acid and methacrylic acid. The combination of references does not

teach the application of a drug eluting polymer before the application of the polymer having functional groups, wherein the drug is chosen from a group of anti-inflammatory, anti-proliferative, anti-migratory or immunosuppressive agents. The drug eluting polymer is not taught to be applied by immersion or spraying, with a thickness of 0.5 and 20 microns. The combination of references does not teach application of a further biodegradable polymer layers over said biological molecule layer.

The '029 patent teaches an implantable medical device having a structure adapted for introduction into a patient wherein the structure is composed of a base material positioned over the structure. The implantable medical device further includes at least one composite layer of a bioactive agent and a polymer material and at least a barrier layer positioned over the composite layer and being of thickness adequate to provide a controlled release (abstract). The implantable medical device provides a controlled release of at least one bioactive agent into the vascular or other system, or other location in the body, into which the stent or medical device is positioned (column 2, lines 40-45). The implantable medical device of the invention comprises at least one composite layer of bioactive agent and a polymer material and at least one barrier layer positioned over the composite layer or layers. The barrier layer has a thickness adequate to provide a controlled release of bioactive material. The barrier layer is applied to the medical device by a low energy plasma polymerization process. The barrier layer can comprise at least one bioactive agent (column 2, lines 48-60). The implantable medical device of the present invention includes at least one layer formed by a composite of at least one bioactive agent and a biocompatible polymeric material.

When multiple polymer-bioactive agent composite layers are used, the layers by contain the same or different bioactive agents and/or the same or different polymer. This depot contributes partially to providing control over the release of the bioactive agent from the medical device (column 5, lines 5-16). The application of the polymer-bioactive agent composite may be accomplished by physical methods such as spraying, dipping and painting (column 5, lines 23-26). The polymer bioactive layer is typically the thickness of 5 to 25 microns (column 5, lines 33-40). The bioactive agent useful in accordance with the present invention may be used singly or in combination. For example, an anti-proliferative agent may be used in combination with another drug, such as an anticoagulant, anti-inflammatory, anti-thrombogenic, etc (column 6, lines 5-13). The biocompatible polymer material can be chosen from a group of polymers which includes polyalkylenes such as polypropylene, polyethylene and high molecular weight polyethylene (column 6, lines 40-45). The multilayer allow for enhanced adhesion of the mixture to the base material. The bioactive agent-polymer composite layer also provides for an effective way of adjusting the amount of the bioactive agent placed on the base material. Also, composite layer provides a co compliant surface for a subsequent barrier layer and aids in maintaining the mechanical integrity of the barrier layer during the expansion of the medical device (column 7, lines 5-11). The purpose of the barrier layer or layers it to provide further controlled release of the bioactive material when the device is positioned in the vascular system. The barrier layer may contain additional bioactive agent which may be the same or different from the bioactive agent of the bioactive agent polymer composite layer (column 7, lines 33-44). The barrier

layer, applied by low energy plasma polymerization process can be aliphatic or aromatic hydrocarbons, acrylic monomers, n-vinyl pyrrolidone, ethylene oxide or a combination thereof. The monomer gas may have functional groups to allow covalent attachment of appropriate drugs by anchoring to these functional groups (column 7, lines 45-60). The barrier layer of the present invention is preferably less than 5000 Å thick (column 8, lines 57-60).

Therefore it would have been prima facie obvious to one or ordinary skill in the art at the time the invention was made to use the cold plasma treatment followed by the addition of a hyaluronic acid active agent to the plasma treated area as taught by the combination of '877 publication, Klein and the '874 publication to deposit the plasma barrier layer containing a bioactive agent over the stent containing a drug eluting polymer as taught by the '029 patent because the barrier layer provides protection during expansion and helps control the release of the bioactive agent as taught by the '029 patent.

Regarding claim 4, the limitation of the precursors of said polymers having carboxylic groups which are chosen from acrylic acid and methacrylic acid is obvious over the barrier layer, applied by low energy plasma polymerization process can be aliphatic or aromatic hydrocarbons, acrylic monomers, n-vinyl pyrrolidone, ethylene oxide or a combination thereof. The monomer gas may have functional groups to allow covalent attachment of appropriate drugs by anchoring to these functional groups (column 7, lines 45-60 and column 11, claim 8) as taught by the '029 patent.

Regarding claim 11, the limitation of the polymer is applied in the form of a film with a thickness of between 0.01 and 10 microns is obvious over the barrier layer of the present invention is preferably less than 5000 Å thick (column 8, lines 57-60) as taught by the '029 patent. The 5000 Å barrier layer taught is equivalent to 0.5 microns. This is within the required film thickness.

Regarding claim 12, the limitation of application of a drug eluting polymer layer before the application of the polymer having a functional groups is obvious over the medical device having a layer of a bioactive agent and polymer material and at least a barrier layer positioned over the composite layer, wherein the barrier layer is applied by low energy plasma (abstract) as taught by the '029 patent.

Regarding claim 13, the limitation of in which said drug is chosen from the group consisting of anti-inflammatory, anti-proliferative and anti-migratory drugs and immunosuprpressive agents is obvious over the bioactive agent useful in accordance with the present invention may be used singly or in combination. For example, an anti-proliferative agent may be used in combination with another drug, such as an anticoagulant, anti-inflammatory, anti-thrombogenic, etc (column 6, lines 5-13) as taught by the '029 patent.

Regarding claims 15 and 16, the limitation of where the drug eluting polymer is a hydrophobic hydrocarbon (elected species), wherein the hydrophobic hydrocarbon is chosen from polystyrene, polyethylene, polybutadiene and polyisoprene is obvious over the biocompatible polymer material can be chosen from a group of polymers which includes polyalkylenes such as polypropylene, polyethylene and high molecular weight

polyethylene (column 6, lines 40-45 and column 10, claim 2) as taught by the '029 patent.

Regarding claim 18, the limitation of said drug which may be incorporated in a drug eluting polymer is applied by means of immersion in a suitable solution or deposited by spraying is obvious over the application of the polymer-bioactive agent composite may be accomplished by physical methods such as spraying, dipping and painting (column 5, lines 23-26) as taught by the '029 patent.

Regarding claim 19, the limitation of which said drug eluting polymer is deposited in the form of a film with a thickness of between 0.5 and 20 microns is obvious over the polymer bioactive layer is typically the thickness of 5 to 25 microns (column 5, lines 33-40) as taught by the '029 patent.

Regarding claim 28, the limitation of the biological molecules are deposited by immersing the medical device in an aqueous solution containing said biological molecules in a concentration of 0.01% to 1% by weight is obvious over drug eluting polymer is applied by means of immersion in a suitable solution or deposited by spraying is obvious over the application of the polymer-bioactive agent composite may be accomplished by physical methods such as spraying, dipping and painting (column 5, lines 23-26) as taught by the '029 patent and all of the above reagents were dissolved in sufficient water to achieve a final HA concentration in the reaction solution of 1% (page 8, paragraph [0061]) as taught by the '877 publication. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to apply the liquid HA solution as taught by the '877 publication by dip coating as taught

by the '029 publication because it is a well know coating method in the art and is taught as applying an active coating by the '029 patent. It would have been prima facie obvious to one of ordinary skill to optimize the percent HA in the coating solution to obtain optimal therapeutic results.

Regarding claim 31, the limitation of application of further biodegradable polymer layers over said biological molecule layer is obvious over the purpose of the barrier layer or layers it to provide further controlled release of the bioactive material when the device is positioned in the vascular system. The barrier layer may contain additional bioactive agent which may be the same or different from the bioactive agent of the bioactive agent polymer composite layer (column 7, lines 33-44). It therefore would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add an additional barrier layer over the heparin containing plasma deposited layer because the additional barrier layer would further control the release of the bioactive material and multiple barrier layers are taught by the '029 patent.

Claims 14 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (publication date: 1995), US 2002/0037874 (publication date 03/27/2002) and US 6,335,029 (patent date: 01/01/2002) as applied to claims 1-4, 12-13, 15-16, 18-19, 25-26 and 31 above, and further in view of WO 99/03854 (publication date: 1/28/1999).

As mentioned in the above 103(a) rejections, all the limitations of claims 1-4, 12-13, 15-16, 18-19, 25-26 and 31 are taught by the combination of the '877 publication, Klein, the '874 publication and the '029 patent. The combination of references does not teach the drug found in claim 14, wherein the drug is present in quantities of 0.001 mg and 10 mg.

The '854 publication teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the '854 publication with the combination of the '877 publication, Klein, the '874 publication and the '029 patent as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis. This meets the limitation of claim 14.

Regarding claims 20-24, the limitation wherein the drug is an anti-inflammatory, and anti-proliferative, and anti-migratory and an immunosuppressant is met as the addition of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-

pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is taught to the drug eluting polymer. Applicant, in electing the above mentioned drug, indicated that it read on claims 20-24, therefore the elected drug would include the anti-inflammatory, and anti-proliferative, and anti-migratory and immunosuppressant properties. Regarding the limitation where in 0.01 mg to 10 mg of the drug are present per device, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to optimize the amount of drug present on a device to obtain the optimal therapeutic concentration and release of the drug. The recited variants would have been obvious unless there is evidence of the criticality or unexpected results.

Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (publication date: 1995), US 2002/0037874 (publication date 03/27/2002) and US 6,335,029 (patent date: 01/01/2002) as applied to claims 1-4, 12-13, 15-16, 18-19, 25-26 and 31 above, and further in view of US 6,287,285 (patent date: 10/11/2001).

As mentioned in the above 103(a) rejections, all the limitations of claims 1-4, 12-13, 15-16, 18-19, 25-26 and 31 are taught by the combination of the '877 publication, Klein, the '874 publication and the '029 patent. The combination of references does not a preliminary step of cleaning/washing the medical device.

The '285 patent teaches a hydrophilic coating which strongly adheres to a surface of a medical device, or a therapeutic or diagnostic coating strongly, but potentially releasably, adhered to the surface of a medical device (column 1, line 65 to

column 2, line 5). The invention is directed to a method of providing a coating on an intracoprporeal medical device. A durable coating is provided on the medical device which modifies the device surface with a therapeutic, diagnostic, lubricious or other active agent. The coating may be used for a variety of medical devices including stents, catheters, guide wires, cardiac pacing leads and vascular grafts (column 2, lines 10-13). The coating on the medical device generally includes a base coat and a top coat. The base coat has binding component and is used to strongly adhere to the surface of the device (column 2, line 12-18). In the presently preferred embodiments, the device is a polymeric catheter, or a metal guidewire coating with a primer or without a primer, having a hydrophilic coating (column 13, lines 24-30). The surface of the device is generally cleaned before coating with the primer or the hydrophilic coating solutions (column 13, lines 33-36).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to clean the medical device and apply a primer coating to a medical device as taught by the '285 patent before the addition of the drug eluting polymer, plasma treatment and hyaluronic acid coatings as taught by the combination of the '877 publication, Klein, the '874 publication and the '029 patent because it is well known in the art to clean a device for implantation before coating and the addition of the primer coating helps the coating adhere strongly to the medical device as taught by the '285 patent. This meets the limitations of claims 29 and 30.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0087877 (publication date: 05/08/2003) in view of Klein (Water-soluble poly(acrylamide-allylamide) derivatives of saccharides for protein-saccharide binding studies, publication date: 1995) and US 2002/0037874 (publication date 03/27/2002) as applied to claims 1-3 and 25-26 above, and further in view of Tsai (Decomposition of CH_3SH in a RF Plasma Reactor: Reaction Products and Mechanisms, publication date: 2001).

As mentioned in the above 103(a) rejection, all the limitations of claims 1-3 and 25-26 are taught by the combination of the '877 publication, Klein and the '874 publication. The combination of references does not teach the precursor of said polymer having sulphhydryl groups which are chosen from volatile mercaptans.

Tsai teaches application of RF (radio frequency) cold plasma method to the decomposition of methanethiol (methyl mercaptan, CH_3SH) at various input powers (20-90 W) (abstract). Recently, trends toward a higher quality, finer patterning and insulating ability in thin films have let to the application of radio-frequency (RF) plasma technologies (page 2384, second column, second paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use methyl mercaptan as the cold plasma deposited layer as taught by Tsai for the cold plasma deposited layer taught by the combination of the '877 publication, Klein and the '874 publication because use of the methyl mercaptan would leave a free reactive group as is a well known plasma treatment

starting material to those of ordinary skill in the art. This meets the limitations of claim 5.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYNDSEY BECKHARDT whose telephone number is (571)270-7676. The examiner can normally be reached on Monday thru Thursday 7:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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LMB

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